REMARKS

It is our understanding that the proposed amendments filed in response to the Final Office Action will be entered as of right upon entry of the RCE. Therefore, the present listing of the claims shows changes relative to the claims as proposed in the previous response.

Claims 8-16, 28, 31, 33, 34 and 36 are currently pending in the application. Claim 28 is amended. Furthermore, incorrectly labeled claim identifiers from the previously filed response have been corrected. The following amendment is being filed in response to a telephonic discussion with Examiner Woitach on November 15, 2004, and the Advisory Action mailed on November 22, 2004. The Advisory Action stated that newly proposed or amended claims 8-16, 31, 33, 34 and 36 would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claims. The amendments find support in the specification and are discussed in the relevant sections below. No new matter is added.

The Advisory Action states that the embodiments of claim 28 for the particular conditions are new and have not been considered previously. The Action further states that a search would be required and specific consideration for the metes and bounds of the claim for those particular conditions is required.

With this Amendment, Applicants have amended claim 28 to recite:

28. A diagnostic reagent comprising at least one detectably labeled nucleic acid probe of **15 to 50 bases** which hybridizes in **a solution containing 6X SSC, 5x Denhardt's, 1 % SDS (sodium dodecyl sulphate), 0.1 M Na^+ pyrophosphate and 0.1 mg/ml denatured salmon sperm DNA** at 65°C to a sequence selected from the group consisting of any one of SEQ ID NOs 1, 3 or 5. (emphasis added)

As acknowledged previously by the Examiner (page 4, line 10 of the After Final Rejection, mailed on March 22, 2004), support for a fragment of between 15 and 50 bases in length can be found on page 16, last full paragraph of the specification. Furthermore, support for the hybridization conditions recited within claim 28 (i.e., 6X SSC, **5x Denhardt's, 1 % SDS**

(sodium dodecyl sulphate), 0.1 M Na^+ pyrophosphate and 0.1 mg/ml denatured salmon sperm DNA) can be found on page 16, second paragraph.

With this Amendment, Applicants have made an earnest effort to respond to all issues raised during the telephonic discussion and subsequent Advisory Action, and to place all claims presented in condition for allowance. Applicants submit that in view of the preceding remarks, all issues relevant to patentability raised in the Office Action have been addressed. Applicants respectfully request the withdrawal of rejections over the claims of the present invention. If the Examiner believes that a telephone conversation with Applicant's attorney would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney of record.

Respectfully submitted,

Date: January 20, 2005

Barbara A. Deyoe (34,614) for
Kathleen Williams

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/484,629	01/18/2000	Iain Clive Andrew Franklin Robinson	~~3266/85705~~	9911

29933 7590 11/22/2004

18396/1140

PALMER & DODGE, LLP
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BOSTON, MA 02199

EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Docketed
Response Due Appeal Brief due
Statutory Period 12/20/04 (4/20/05 sp)
Palmer & Dodge LLP
Patent Department

Advisory Action	Application No.	Applicant(s)	
	09/484,629	ROBINSON ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 20 September 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on *20 September 2004*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☒ The proposed amendment(s) will not be entered because:

   (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☒ they raise the issue of new matter (see Note below);

   (c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☒ Newly proposed or amended claim(s) *8-16,31,33,34 and 36* would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *8-16,28,31,33,34 and 36*.

   Claim(s) withdrawn from consideration: *29 and 35*.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

Joe Woitach
AU1632

Continuation of 2. NOTE: the embodiments of claim 28 for the particular conditions are new and have not been considered previously. A new search would be required and specific consideration of the metes and bounds of the claim for those particular conditions is required.

Continuation of 5. does NOT place the application in condition for allowance because: the claim amendments have not been entered, and the arguments regarding the claims are not applicable to pending claims.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/484,629	01/18/2000	Iain Clive Andrew Franklin Robinson	3265/85705	9911

29933 7590 03/22/2004

PALMER & DODGE, LLP
KATHLEEN M. WILLIAMS
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BOSTON, MA 02199

COPY

EXAMINER	
WOITACH, JOSEPH T	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

FINAL

Docketed
Response Due Resp to Final OA
Statutory Period 6/22/04 (9/22/04)
Palmer & Dodge LLP ESP
Patent Department

Office Action Summary

Application No.	Applicant(s)	
09/484,629	ROBINSON ET AL.	
Examiner	**Art Unit**	
Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-16,28,31,33,34 and 36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-16, 28 and 31, 33, 34 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is an original application filed January 18, 2000, which claims benefit to foreign applications: PCT/GB99/02658, filed December 8, 1998; 9817566.4, filed August 12 1998; and 9910522.3, filed May 6, 1999, all filed in the United Kingdom.

As noted in prior office action mailed December 11, 2003, the specification has been amended. Claims 8-10, 16, 28, and 31-34 were amended. Claims 30, 32 and 35 were cancelled. Claim 36 was added.

Applicants' amendment filed January 11, 2004, has been received and entered. The specification has been amended. Claims 8-16, 28 and 31, 33-36 are pending.

Election/Restriction

Newly submitted claim 36 is directed to Applicants elected invention. Applicants have elected group II, drawn to a nucleic acid encoding a 5'OT-EST polypeptide, a vector containing said nucleic acid and a cell containing said vector (see paper number 11 and 15).

As indicated in the previous office action, claim 35 is directed to a method of using a 5'OT-EST for determining mutations, polymorphisms or other changes. Claim 35 has been withdrawn from consideration as being directed to a non-elected invention (see 37 CFR 1.142(b) and MPEP § 821.03).

Claims 8-16, 28 and 31, 33, 34 and 36 are currently under examination.

Sequence compliance

The objection to the specification because the application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2), and specifically, Figure 6 contains multiple sequences which are not identified in the figure of the short description of the figure is withdrawn.

The amendments to the specification have obviated the basis of the rejection.

Claim Objections

Claim 32 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn.

Cancellation of claim 32 has rendered the rejection moot.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 28 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn.

The amendment to claim 28 to recite "5 to 150" which is supported by the instant specification has obviated the basis of the rejection.

Newly added claim 36 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application". In the instant case, a nucleic acid probe 'of 10 to 50 nucleotides in length' is considered new matter. Applicants have not specifically pointed to the portion of the specification for support of this amendment. Upon review of the specification literal support for this amendment can not be found. Support for a probe which is preferably 5 to 150 nucleotides is found on page 15, second to last paragraph. On page 16, last full paragraph support for a fragment that is 'between 15 and 50 bases in length" is found. Additionally, the literal support in the specification is not specifically associated with a probe to detect mutations or polymorphisms which predispose an individual to obesity, rather it is only associated with sequences which are related to fragments which encode a polypeptide. The only size fragment literally supported by the specification is 'about 20 bases in length" for use in PCR reactions (page 16, last paragraph).

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claim 36 is also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure".

Claims 8-16, 28, 31, 33 and 34 stand rejected and newly added claim 36 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants note the amendments to the claims, in particular clause (b) indicates sequence that hybridize and have a defined function (pages 9-10). Further, Applicants note that the specification provides details for "stringent hybridization" (bottom of page 10). With regard to the limitation that an amino acid sequence "modulates the obesity of an animal" Applicants cite the Examiners comments on the results of the J17 and J45 lines presented in the instant

specification and argue that this interpretation is not correct (page 11). Contrasting the phenotype of other models where GH expression has been characterized, Applicants argue that there is a clear correlation with the 5'OT-EST sequence. (bottom of page 11 to page 12). Given the description of the structural/functional limitations requiring hybridization and the correlation with the ability to modulate obesity in an animal Applicants argue that claims as amended are supported by adequate written description (page 12). See Applicants' amendment, pages 9–12. Applicants' arguments have been fully considered, but not found persuasive.

The amendments to the claims are noted, in particular that the sequences encompassed by the claims now include any sequence that hybridizes to SEQ ID NOs: 1, 3, 5 or 7 and encodes a protein that has the ability to modulate obesity in an animal. Initially, Examiner does not dispute the results presented in the present specification and acknowledges that the expression of 5'OT-EST sequence is associated with obesity, and that the phenotype is different from that associated with the expression of GH. The basis of the instant rejection focuses on the breadth of the sequences encompassed by the claims. More specifically, the claims encompass (as set forth in clause (b)) any sequence that will hybridize to SEQ ID NOs: 1, 3, 5 or 7 as it is related to structure and of that structural limitation only the sequences associated with obesity in an animal as it is related to function. The issue is the failure of the specification to describe adequately of which sequences are identified that hybridize, which will meet the functionally limitations required by the claims. It is noted that adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). In the instant case, the specification is silent with respect to any critical characteristic of a sequence

which would be considered a 5'OT-EST. Further, beyond the specific SEQ ID NOs defined to be a 5'OT-EST sequence, the specification is silent with respect to what would be considered a mutation or a polymorphism of these specific sequences. Moreover, the specification fails to provide a clear nexus between the SEQ ID NOs and there consequence on any assayable phenotype of a cell or transgenic animal wherein the artisan could even test any variation of the SEQ ID NO. Again, it is not disputed that the full length cDNA sequences identified in mouse, human and rat are associated with obesity, however the breadth of the claims is very large encompassing any sort of variant including mutants, truncations, entire gene sequences and any polymorphic sequence that would hybridize under a given set of conditions. The specification does not disclose all these possible embodiments, and even if the structural limitation could be adequately defined by hybridization (see rejection under 35 USC 112, second paragraph), importantly among all these embodied sequences there is no guidance to which would meet the functional limitations of the claims. The specification is silent with respect to any mutation or polymorphism which is associated with obesity. For example, claims 33 and 34 recite a specific short sequences however these sequences alone are not capable of modulating obesity, even though they may meet the functional limitation of the claims. More simply put given any linear polynucleotide or amino acid sequence the specification fails to provide the necessary guidance to determine whether that particular sequence is functional, and given the uncertainty of the hybridization conditions whether it even meets the structural limitations as well.

Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). In the instant case, the

specification is silent with respect to any critical characteristic of a sequence which would be considered a 5'OT-EST. Further, beyond the specific SEQ ID NOs defined to be a 5'OT-EST sequence from three different species of mammal, the specification is silent with respect to what would be considered a mutation or a polymorphism of these specific sequences. Finally, the specification fails to provide a clear nexus between the SEQ ID NOs and there consequence on any assayable phenotype of a cell or transgenic animal wherein the artisan could even test any variation of the SEQ ID NO. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed."*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1116. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.*, 48 USPQ2d 1641, 1646 (1998). In the instant case, the specification fails to provide any specific or identifying features of a 5'OT-EST beyond the specific sequences set forth as SEQ ID NOs. Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Since the specification is silent with respect to any relevant identifying characteristic of a 5'OT-EST (neither for the polynucleotide nor the polypeptide sequences) the specification

fails to provide any nexus between structure and function of a 5'OT-EST which the artisan could use to determine if a sequence with any given structural limitation would be considered a 5' OT-EST.

Possession may be shown by clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Because the specification fails to provide any identifying characteristics of the 5'OT-EST sequence its fails to provide an adequate description demonstrating that Applicants were in possession of the invention as broadly claimed. Therefore, for the reasons above and of record, the rejection is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8-16, 28, 31, 33, 34 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Initially, claims 8, 9, 10, 16 and 28 rejected for being are vague and indefinite in the recitation of 'at least 90% homologous... as determined by BLAST analysis using default parameter' is withdrawn. The amendment to the claims to delete this embodiment has obviated the basis of the rejection. With respect to claims 9 and 28, it is noted that the new sequence listing provides nucleic acid sequences for SEQ ID NOs: 5, 7, 16 and 17 and therefore, the rejection is withdrawn.

Claims 8-16, 28, 31, 33, 34 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, claims 8-10, 16 and 28 have been amended to recite nucleic acid sequences "that hybridize under stringent hybridization conditions". The specification provides only a reference to conditions considered to be stringent (page 16, second paragraph) and teach that a variety of modifications can be made and are contemplated for hybridization and the conditions must be determined empirically based on the probe use (page 16, fifth paragraph). The metes and bounds of the claims are indefinite because conditions considered stringent are not clearly set forth. As taught by the specification multiple conditions exist, and 'optimal conditions' must be determined empirically, thus what one would consider "stringent" would vary from one individual to another. Dependent claims merely set forth that the sequences are in a vector or transformed into a cell. Claims 33, 34 and 36 set forth structural limitations of the sequences (specific sequences and a specific range of length), however this fails to further define the conditions in which these limitations would be detected or more specifically define the hybridization conditions encompassed by the claims.

Conclusion

No claim is allowed.

The claims are free of the art of record because the art fails to teach or make obvious the specific SEQ ID NOs or sequences that hybridize and have a specific activity as encompassed by

the present claims. It is noted that GenBank sequence entries: AA955566, AA421393, AA505752, AA421310, AA2422211, AA245389, AA104183, AA850004, H31115, or H31114 (previously applied) would likely hybridize, however because the sequences are EST sequences they represent truncated proteins that would not modulate obesity in an animal.

The TO and AVP genomic sequences have been previously described, however these cloned sequences did not contain the 5' polynucleotide sequence which comprised the 5'OT EST gene described in the instant specification. Further, the prior art teaches that ESTs sharing partial homology to the 5'OT EST sequences were known, however the art failed to teach the full length sequences as presently disclosed, and failed to appreciate the presence of the 5'OT EST gene 13 kb upstream of the TO gene, or provide motivation to link this gene or gene product described only by the partial EST sequences with the TO gene. The OT sequences described are demonstrated to be in physical linkage to Ptpra, AVp and Oxt and provide physical markers of these genes on chromosome 2 (specification-page 9).

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (571) 272-0734.

Any inquiry of a general nature or relating to the status of this application should be directed to Rene Jones at 571-272-0547.

Joseph T. Woitach

/Joe Woitach/
AU1632

Atty. Docket No.: 18396/1140 PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Robinson, et al.	Examiner:	Woitach, J.
Serial No.:	09/484,629		
Filed:	January 18, 2000	Group Art Unit:	1632
Entitled:	Obesity Gene		
		Conf. No.:	9911

CERTIFICATE OF MAILING UNDER 37 CFR 1.10

I hereby certify that the paper (and any paper or fee referred to as being enclosed) is being deposited with the United States Postal Service using Express Mail to Addressee Service, under 37 C.F.R. Section 1.10, **Express Mail Label No. EV 242755674 US** on this date, September 20 2004, postage prepaid, in an envelope addressed to Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Kathleen M. Williams
Name of Person Mailing Paper

Signature of Person Mailing Paper

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT AFTER FINAL REJECTION UNDER 37 C.F.R. 1.116

Sir:

This Amendment After Final Rejection is being filed in response to the Final Office Action mailed from the U.S. Patent and Trademark Office on March 22, 2004, in the above-identified application.

An extension of time and a Notice of Appeal from the Final Office Action dated March 22, 2004, with appropriate fees, are being filed concurrently.

Amendments to the Claims are shown in the "Listing of the Claims" which begins on page 2 of this paper.

Remarks begin on page 5 of this paper.

Applicants respectfully request entry of the amendments and remarks.

The following Listing of the Claims will replace all prior versions and all prior listings of the claims in the present application:

Listing of the Claims:

1 – 7. (Withdrawn)

8. (Currently amended) A nucleic acid encoding a 5'OT-EST polypeptide comprising an amino acid sequence selected from the group consisting of:

~~(a)~~ the sequences set forth in any one of SEQ ID Nos. 2, 4, or 6. ~~; and~~

~~(b) an amino acid sequence encoded by a nucleic acid that hybridizes under stringent hybridization conditions to any one of SEQ ID Nos. 1, 3, 5 or 7, or to the complement thereof, wherein said encoded amino acid sequence modulates the obesity of an animal~~.

9. (Currently amended) The nucleic acid of claim 8, having a sequence selected from the group consisting of SEQ. ID. Nos. 1, 3, 5, 7, 16 or 17~~, or a nucleic acid sequence that hybridizes under stringent hybridization conditions to any one of said sequences, or to the complement thereof,~~ wherein a polypeptide encoded by a said nucleic acid sequence modulates the obesity of an animal.

10. (Currently amended) The nucleic acid of claim 9, comprising the sequence with SEQ ID NO: 31 ~~or a nucleic acid sequence that hybridizes under stringent hybridization conditions to SEQ ID NO: 31, or to the complement thereof~~.

11. (Previously amended) A nucleic acid vector comprising a nucleic acid sequence of any one of claims 8 to 10.

12. (Previously amended) The vector of claim 11, wherein said vector is a cosmid vector.

13. (Previously amended) The vector of claim 11 or 12 further comprising one or more sequences selected from the group consisting of sequences of the coding region of the

oxytocin (OT) gene, the coding region of the vasopressin (AVP) gene, or the coding region of the human growth hormone (hGH) gene.

14. (Previously amended) A vector of claim 12, wherein said vector has the structure of cVO14 as set forth in Figure 4 (SEQ. ID. No. 17).

15. (Previously amended) A cell transformed with a vector of any one of claims 11 to 14.

16. (Currently amended) A method for producing a 5'OT-EST polypeptide having a sequence selected from the group consisting of (a) the sequences set forth in any one of SEQ ID Nos. 2, 4, 6~~, or (b) an amino acid sequence encoded by a nucleic acid that hybridizes under stringent hybridization conditions to any one of SEQ ID Nos. 1, 3, 5 or 7, or to the complement thereof~~, wherein said encoded amino acid sequence modulates the obesity of an animal, the method comprising transforming a cell with a vector of any one of claims 11 to 14 and culturing the cell to produce the polypeptide.

17-27. (Withdrawn)

28. (Currently amended) A diagnostic reagent comprising at least one detectably labeled nucleic acid probe of 5 to 150 nucleotides which hybridizes ~~under stringent hybridization conditions~~ <u>in 1M Na^+ at 65°C</u> to a sequence selected from the group consisting of ~~(a)~~ any one of SEQ ID NOs 1, 3 or 5~~, and (b) a nucleic acid sequence that encodes a polypeptide that modulates the obesity of an animal and that hybridizes under stringent hybridization conditions to any one of SEQ ID NOs 1, 3 or 5 or the complement thereof~~.

29. (Withdrawn)

30. (Cancelled)

31. (Previously amended) The nucleic acid of claim 8, wherein said 5'OT-EST polypeptide, in vivo, modulates the obesity of an animal which expresses said 5'OT-EST polypeptide.

32. (Cancelled)

33. (Previously Amended) The nucleic acid of any one of claims 8~~, 30,~~ or 31 wherein said 5'OT-EST polypeptide comprises the sequence of SEQ ID NO: 37.

34. (Previously Amended) The nucleic acid of any one of claims 8~~, 30,~~ or 31 wherein said 5'OT-EST polypeptide comprises the sequence of SEQ ID NO: 8.

35. (Withdrawn)

36. (Previously Added) The diagnostic reagent of claim 28 wherein said at least one detectably labeled nucleic acid probe is 10 to 50 nucleotides in length.

REMARKS

Claims 8-16, 28, 31, 33, 34 and 36 are currently pending in the application. Claims 8, 9, 10, 16, 28 and 36 are amended. The amendments find support in the specification and are discussed in the relevant sections below. No new matter is added.

Claim 36 is rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 36 is also rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described. The Examiner states that:

> "In the instant case, a nucleic acid probe 'of 10 to 50 nucleotides in length' is considered new matter. Applicants have not specifically pointed to the portion of the specification for support of this amendment. Upon review of the specification literal support for this amendment can not be found. Support for a probe which is preferably 5 to 150 nucleotides is found on page 15, second to last paragraph. On page 16, last full paragraph support for a fragment that is 'between 15 and 50 bases in length' is found. Additionally, the literal support in the specification is not specifically associated with a probe to detect mutations or polymorphisms which predispose an individual to obesity, rather it is only associated with sequences which are related to fragments which encode a polypeptide. The only size fragment literally supported by the specification is 'about 20 bases in length" for use in PCR reactions (page 16, last paragraph)."

Applicants respectfully disagree. Applicants submit that literal support for a probe of between 10 and 50 nucleotides can be found within page 17, last paragraph of the specification:

> "As used herein, a **probe is e.g. a single-stranded DNA or RNA that has a sequence of nucleotides that includes between 10 and 50**, preferably between 15 and 30 and most preferably at least about 20 contiguous bases that are the same as (or the complement of) an equivalent or greater number of contiguous bases set forth in SEQ ID Nos. 1, 3 and/or 5."

Furthermore, as previously acknowledged by the Examiner, support for between 15 and 50 bases in length is also found within the specification. Applicants further submit that additional support for a probe is found within the same paragraph:

> "Advantageously, it is about 25 bases in length, preferably about 20 bases in length. For differentiating between mutant and wild type 5'OT-EST by PCR reactions, 20mers are the preferred size, whilst for use as probes in, for example, Southern hybridisation, the use of 40mers is preferred."

Other support for probes between 10 and 50 bases in length can also be found within the specification. Described probes, SEQ ID NO:18 – SEQ ID NO:29, vary in length from 18 bp to 25bp. Other aspects of the probe are also disclosed, such as an alignment among 5'OT-EST from human, rat and mouse (Figure 6), how to synthesize nucleic acids (page 17, third paragraph) and its analogs (page 19, paragraph five – page 20, paragraph 2), hybridization conditions (page 16, paragraph 1 – paragraph 5), labeling of the probe (page 18, second paragraph), detecting hybridization (page 18, last paragraph). In light of the extensive support within the specification on probes, Applicants submit that claim 36 is enabled. In light of the foregoing, Applicants respectfully request withdrawal of the §112, first paragraph rejection and reconsideration of the claim 36.

Claims 8-16, 28, 31, 33 and 34 stand rejected and newly added claim 36 is rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the invention was filed, had possession of the claimed invention. The Office Action states:

> "The basis of the instant rejection focuses on the breadth of the sequences encompassed by the claims. More specifically, the claims encompass (as set forth in clause (b)) any sequence that will hybridize to SEQ ID NOs: 1, 3, 5, or 7 as it is related to structure and of that structural limitation only the sequences associated with obesity in an animal as it is related to function. The issue is the failure of the specification to describe adequately of which sequences are identified that hybridize, which will meet the functionally [sic] limitations required by the claims."

"In the instant case, the specification is silent with respect to any critical characteristic of a sequence which would be considered a 5'OT-EST. Further, beyond the specific SEQ ID NOs defined to be a 5'OT-EST sequence, the specification is silent with respect to what would be considered a mutation or polymorphism of these specific sequences. Moreover, the specification fails to provide a clear nexus between the SEQ ID NOs and there [sic] consequence on any assayable phenotype of a cell or transgenic animal wherein the artisan could even test any variation of the SEQ ID NO. Again, it is not disputed that the full length cDNA sequences identified in mouse, human and rat are associated with obesity, however, the breadth of the claims is very large encompassing any sort of variant including mutants, truncations, entire gene sequences and any polymorphic sequence that would hybridize under a given set of conditions. The specification does not disclose all these possible embodiments, and even if the structural limitation could be adequately defined by hybridization (see rejection under 35 U.S.C. 112, second paragraph), importantly among all these embodied sequences there is no guidance to which would meet the functional limitations of the claims. The specification is silent with respect to any mutation or polymorphism which is associated with obesity. For example, claims 33 and 34 recite a specific short sequences however these sequences alone are not capable of modulating obesity, even though they may meet the functional requirements of the claims. More simply put given any linear polynucleotide or amino acid sequence the specification fails to provide the necessary guidance to determine whether that particular sequence is functional, and given the uncertainty of the hybridization conditions whether it even meets the structural limitations as well."

"In the instant case, the specification is silent with respect to any critical characteristic of a sequence which would be considered a 5'OT-EST. Further, beyond the specific SEQ ID NOs defined to be a 5'OT-EST sequence from three different species of mammal, the specification is silent with respect to what would be considered a mutation or a polymorphism of these specific sequences. Finally, the specification fails to provide a clear nexus between the SEQ ID NOs and there[sic] consequence on any assayable phenotype of a cell or transgenic animal wherein the artisan could even test any variation of the SEQ ID NO."

"In the instant case, the specification fails to provide any specific or identifying features of a 5'OT-EST beyond the specific sequences set forth as SEQ ID NOs. Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Since the specification is silent with respect to any relevant identifying characteristic of a 5'OT-EST (neither for the polynucleotide nor the polypeptide sequences) the specification fails to provide any nexus between structure and function of a 5'OT-EST which the artisan could use to determine if a sequence with any given structural limitation would be considered a 5'OT-EST."

> "Possession may be shown by clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Because the specification fails to provide any identifying characteristics of the 5'OT-EST sequence it fails to provide an adequate description demonstrating that Applicants were in possession of the invention as broadly claimed. Therefore, for the reasons above and of record, the rejection is maintained."

Without acquiescing to the Examiners statement, Applicants have amended claims 8-10 and 16 so that they no longer claim sequences that hybridize under stringent hybridization conditions to the sequences provided with SEQ ID NOs. For example, claim 8 recites:

> 8. A nucleic acid encoding a 5'OT-EST polypeptide comprising an amino acid sequence selected from the group consisting of the sequences set forth in any one of SEQ ID Nos. 2, 4, or 6.

Furthermore, Claim 28 has been amended to remove clause (b):

> 28. A diagnostic reagent comprising at least one detectably labeled nucleic acid probe of 5 to 150 nucleotides which hybridizes under stringent hybridization conditions in 1M Na^+ at 65°C to a sequence selected from the group consisting of any one of SEQ ID NOs 1, 3 or 5.

Applicants have amended claims 8-10, 16 and 28 solely to expedite prosecution of the instant application. As currently amended, Applicants submit that the specification provides sufficient written description to support claims 8-16, 28, 31, 33 and 34, and therefore respectfully request withdrawal of the §112, first paragraph rejection and reconsideration of the claims.

Claims 8-16, 28, 31, 33, 34 and 36 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Office Action states:

> "claims 8-10, 16 and 28 have been amended to recite nucleic acid sequences "that hybridize under stringent hybridization conditions". The specification provides only a reference to conditions considered to be stringent (page 16, fifth paragraph). The metes and bounds of the claims are indefinite because conditions considered stringent are not clearly set forth. As taught by the specification multiple conditions exist, and 'optimal conditions' must be determined empirically, thus what one would consider "stringent"

would vary from one individual to another. Dependent claims merely set forth that the sequences are in a vector or transformed into a cell. Claims 33, 34 and 36 set forth structural limitations of the sequences (specific sequences and specific range of length), however this fails to further define the conditions in which these limitations would be detected or more specifically define the hybridization conditions encompassed by these claims."

With this amendment, Applicants have amended claims 8-10 and 16 so that they no longer recite "sequences that hybridize under stringent hybridization conditions", and therefore traverse this rejection. Applicants have further amended claim 28 to cite specific hybridization conditions: 1M Na^+ at 65°C:

28. A diagnostic reagent comprising at least one detectably labeled nucleic acid probe of 5 to 150 nucleotides **which hybridizes in 1M Na^+ at 65°C** to a sequence selected from the group consisting of any one of SEQ ID NOs 1, 3 or 5. (emphasis added)

Support for hybridization at 1M Na^+ at 65-68°C is found on page 16, paragraph 2. As such, Applicants submit that claims 8, 16 and 28, as well as dependent claims 9-15, 31, 33, 34 and 36 are definite. As such, Applicants respectfully request withdrawal of the §112, second paragraph rejection and reconsideration of the claims.

With this Amendment, Applicants have made an earnest effort to respond to all issues raised in the Office Action of May 24, 2004, and to place all claims presented in condition for allowance. Applicants submit that in view of the preceding remarks, all issues relevant to patentability raised in the Office Action have been addressed. Applicants respectfully request the withdrawal of rejections over the claims of the present invention. If the Examiner believes that a telephone conversation with Applicant's attorney would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney of record.

Respectfully submitted,

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